



### ABSTRACT

The present invention relates to therapeutic and diagnostic methods and compositions based on Notch proteins and nucleic acids. The invention provides for treatment of disorders of cell fate or differentiation by administration of a therapeutic compound of the invention. Such therapeutic compounds (termed

5 herein "Therapeutics") include Notch proteins and analogs and derivatives (including fragments) thereof, antibodies thereto, nucleic acids encoding the Notch proteins, analogs, or derivatives, Notch antisense nucleic acids, as well as toporythmic proteins and derivatives which bind to or otherwise interact with Notch proteins and their encoding nucleic acids and antibodies. In a preferred

10 embodiment, a Therapeutic of the invention is administered to treat a cancerous condition, or to prevent progression from a pre-neoplastic or non-malignant state into a neoplastic or a malignant state. In other embodiments, a Therapeutic is administered to treat a nervous system disorder or to promote tissue regeneration and repair. In one embodiment, Therapeutics which antagonize, or inhibit, Notch

15 function (hereinafter "Antagonist Therapeutics") are administered for therapeutic effect. In another embodiment, Therapeutics which promote Notch function (hereinafter "Agonist Therapeutics") are administered for therapeutic effect. Diagnostic methods and methods of inhibiting Notch expression are also provided.

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